SUCCESSFUL AGING

Memory, Thinking, and Aging What We Know About What We Know

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Cognition is the foundation that underlies all daily activities, from the most basic to the most complex. Successful aging depends, in large part, on maintaining a level of cognitive ability that allows a person to interact effectively and appropriately with the environment. In the following article we provide an overview of the effects of aging on cognition; discuss physical, social, and psychological factors that have been shown to influence cognition in old age; and review current literature on interventions that may optimize successful cognitive aging. We conclude with a discussion of abnormal cognitive aging and review current research on risk factors and treatments of Alzheimer's disease and other dementing illnesses.

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Levery action of every day is mediated and influenced by our cognitive abilities. From the most sophisticated human activity to the most mundane, everything we do depends on our capacity to understand and interact with our environment. Our ability to interact with those around us, converse, successfully solve daily problems, and even dress, bathe, toilet, and feed ourselves all depend on our level of cognitive function. Consequently, successful cognitive aging is an essential substratum of successful aging.

Cognitive health does not exist in isolation. Quite the contrary, it influences, and is influenced by, an array of medical, social, affective, and functional changes that often occur with increased age. For example, it is well known that a host of medical diseases and medications can adversely influence cognitive abilities in older adults. Conversely, impaired cognition may cause older adults to misunderstand their physicians' instructions, to take their medications improperly, and to have generally more difficulty complying with preventive and secondary health regimens.

Rather than being unidimensional, cognitive health is multidimensional. It encompasses an array of functions, including general intellectual ability, memory, language, visual-spatial skills, perception, and complex problem solving. Each of these areas represents complex domains. For example, the term "memory" refers to a diverse array of activities, including the abilities to remember past events (remote memory), learn new information (recent memory), remember future events (prospective memory), perform familiar activities (procedural memory), and learn without directed effort (incidental memory).

Consequently, successful cognitive aging must be defined in such a way as to take into account the interactive and multifaceted nature of cognitive function. Several definitions have been proposed to attempt to capture the concept of successful cognitive aging. Some have defined "successful" as the upper strata of cognitive functioning. 1.2 According to these authors, only those persons who score substantially above the mean (defined in various ways) are aging successfully. Others have defined "successful" as having minimal interruption of usual function. 3-7 This latter definition reflects a more interactional approach and suggests that success reflects the extent to which a person is able to interact effectively with the environment and adapt to age-related changes.

In this article, we will adhere to this multifaceted and interactive definition: successful cognitive aging is the

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ABBREVIATIONS USED IN TEXT

EPESE = Established Population for the Epidemiologic Study of the Elderly SLS = Seattle Longitudinal Study

interplay between cognitive status and a person's ability to adapt, accommodate, and adjust to the environment. In so doing, we think we provide a definition of the most direct relevance to older adults and their health care practitioners. We will survey the cognitive-aging literature, beginning with an overview of what is known about the areas of cognition likely to be affected by increasing age and those unlikely to be affected. We will then discuss the factors known to influence cognitive functioning in old age, concentrating on three areas that are the primary focus of current empiric research on successful aging, namely, physical, social, and psychological health. Once we understand what areas of cognition are affected by age and what mediates those effects, the next logical step is to identify what can be done to optimize successful cognitive aging. To answer this question, we turn to the intervention literature. By far, most intervention research has emphasized memory training, so we will focus primarily on the use of such strategies with older adults.

Finally, considering the factors that might enhance successful aging and mitigate decline naturally leads to a discussion of the dementing disorders of late life because they represent the opposite end of the cognitive aging spectrum. By understanding risk factors for these diseases, we might better understand how to prevent these disorders, ensure optimal function, or both. By understanding what cognitive-enhancing strategies have been investigated in dementia, we may discover useful techniques for improving cognition in nondemented older adults. We will conclude by suggesting directions for future research and avenues of clinical treatment.

Cognitive Changes With Normal Aging

Considerable research has been done on the changes in cognition that are associated with aging. Early work conceptualized general human intellect as having two aspects: crystallized intelligence, which includes overlearned, familiar skills accumulated through education and practice, and fluid intelligence, which includes nonverbal reasoning, motor tasks, and problem-solving abilities that evolve and change as a result of physiologic maturation.^{8,9} It was theorized that crystallized abilities-such as knowledge of general facts and vocabulary—sharply increase during the early years of formal education and then stabilize or gradually improve throughout adulthood. In contrast, fluid abilities improve throughout childhood, then gradually decline in adult years, with more rapid deterioration in old age due to neuronal loss, changes in physiologic brain function, and increased rates of disease and injury. This general intelligence approach has been criticized by adherents of more complex cognitive theories, who say that intellect is a function of many distinct factors that decline at differential rates and that should be considered separately in the evaluation of normal cognitive aging. ¹⁰ Others have argued that psychomotor or cognitive slowing can explain most if not all of the measured changes in performance that are associated with aging. ¹¹

Despite this controversy, both cross-sectional and longitudinal studies have supported the relative stability of verbal abilities with advancing age and the decline in tasks requiring perceptual speed, selective attention, and complex problem solving. 12-14 The largest and most extensively documented study of cognitive changes associated with normal aging is the Seattle Longitudinal Study (SLS),6,15 which has been observing multiple cohorts of aging adults since 1956. More than 3,000 cognitively intact subjects have been enrolled and evaluated every seven years in five cognitive domains: verbal meaning (recognition vocabulary), spatial orientation (ability to rotate objects mentally in two-dimensional space), inductive reasoning (ability to generate novel concepts or relationships), number skills (simple addition), and word fluency (verbal recent memory and word-list generation from lexical categories). The SLS has shown that performance on all cognitive domains begins to decline by age 74, although this is mediated by gender and cohort effects. Specifically, women decline earlier on fluid abilities, whereas men decline sooner on measures of crystallized ability.16 Cohort differences have also been observed in patterns of decline: subsequent generations have showed steady improvement in inductive reasoning, verbal meaning, and spatial orientation during the SLS sampling period, in contrast to declining number skills and, to a lesser extent, declining verbal memory and fluency.16

Considerable consensus exists that important interindividual differences explain age-related cognitive decline. 17-20 In the SLS, few subjects have shown global decline; rather, most participants maintained or increased their level of performance on at least one cognitive domain well beyond 80 years of age, suggesting that successful cognitive aging involves selectively maintaining abilities. 21 When decline does occur, the age of the start of decline varies widely. The reasons for this variation are largely unknown; researchers have suggested that differences between subjects may be due to such factors as genetic predisposition, chronic disease, socioeconomic differences, level of intellectual and environmental stimulation, and personality. 6,10,19,22

Some authors have distinguished between cognitive ability and cognitive competence. The term "competence" is not used here to imply legal capacity for decision making. Rather, it refers to a person's potential to use a combination of personal resources, including past experience, physical and interpersonal skills, and cognitive abilities, to adapt to particular situations.²³ It helps explain why some older adults who score low on neuropsychological tests of complex problem-solving tasks nevertheless remain capable in highly demanding occu-

pations, avocational pursuits, or challenging personal circumstances. Cognitive competence is a useful construct because of its implications for successful aging and remediation. For example, continued late-life involvement in productive activity has been associated with higher levels of physical and cognitive functioning. Cognitively competent older adults who desire to remain productive in paid or volunteer activities may be able to draw on previous experience and interpersonal skills to offset circumscribed age-associated cognitive decline. Even older adults with substantial physical or cognitive limitations can capably pursue personal goals in their own environment when they are allowed access to external aids, social supports, or technologic advances to compensate for age-related losses.

Correlates of Successful Cognitive Aging

In the past ten years, several large multivariate epidemiologic investigations have been conducted in various parts of the United States to identify what factors contribute to the maintenance of cognitive and functional abilities with advancing age. 2.6,17,21,26,27 These studies have focused on three main research areas, namely, the role of physical, social, and psychological health in the maintenance of cognitive function. Although each investigation has defined successful cognitive functioning in a different way and each has assessed different factors that are proposed to be related to cognition, some common themes have emerged.

The first theme has already been described. Persons vary widely in the type and severity of cognitive changes shown with advancing age. For example, in the SLS, few showed global decline; rather, most maintained or improved their level of performance in at least one cognitive domain well beyond 80 years of age. When decline did occur, the age of the start of decline varied widely. Similarly, in the Georgia Centenarian Study, which investigated variables related to cognitive functioning of 165 participants aged 60 to 100, 27 overall intellectual functioning was lower in the oldest cohort, but everyday problem solving remained intact even among the oldest subjects.

Despite this variation, consistent mitigating factors have been identified and replicated across different studies. Educational achievement has been found to be a strong predictor of cognitive functioning in later decades of life. Persons with higher educational levels show less age-related decline. 1,19,22,26,28,29 Educational experiences early in life also appear to exert some protection against the cognitive deterioration associated with dementing illnesses. The SLS found that education was significantly correlated with the maintenance of certain aspects of cognitive function, particularly in the areas of verbal meaning and fluency and inductive reasoning.

Physical health status, including number of illness episodes, chronic disease, exercise participation, and subjective reports of health and health-related activities, such as alcohol and tobacco use, have been consistent-

ly correlated with cognitive function in older adults. ^{1,2,17,26,31} For example, in the SLS, cardiovascular disease was the primary health-related variable predicting cognitive decline. ³¹ Persons with cognitive decline averaged ten times as many hospital admissions for cardiovascular disease as those without decline and had twice as many cardiovascular-related outpatient medical visits. All subjects in this investigation belong to the same health maintenance organization (Group Health Cooperative, Seattle, Washington), which maintains a uniform health care database on all its members. Thus, this investigation provided a unique, objective assessment of health changes in its study participants.

Possibly modifiable health factors including strenuous physical activity, pulmonary function, and cardiovascular status have also been identified as important factors in the maintenance of cognitive ability. For example, another longitudinal study, the Established Population for the Epidemiologic Study of the Elderly (EPESE)-MacArthur Foundation Research Network, evaluated a sample of 4,030 persons aged 70 to 79 years from which 1,192 subjects were identified as "high functioning," based on brief assessments of physical and cognitive status.²⁶ These subjects were compared with age- and sex-matched subjects who were in the "medium" or "low-functioning" groups. High-functioning subjects rated their health much higher, smoked fewer cigarettes, exercised more, and had better pulmonary function than medium or low-functioning subjects.

Emotional state has been found correlated with cognitive function in late life. Self-efficacy (the belief that through one's actions, a person can produce a desired effect), depression, and anxiety have each been significantly associated with cognition. For example, in the EPESE study, the high-functioning elders scored higher on scales of self-efficacy and mastery and reported fewer symptoms of anxiety and depression than lower functioning elders. ²⁶ In EPESE subjects, lower self-efficacy was significantly predictive of greater cognitive decline over a 2 ½ year period. ¹ Mental health was also significantly related to cognitive ability in the Georgia Centenarian Study, ²⁷ in that persons who had higher cognitive ability had lower levels of depression and anxiety.

In summary, age-related cognitive decline is variable, but factors influencing decline have been identified and replicated across the different groups studied. Previous educational achievement was consistently one of the strongest predictors of cognitive functioning in the later decades of life, with more education mitigating decline in late life. Physical status has been consistently correlated with cognitive function, including such potentially modifiable factors as strenuous physical activity, pulmonary function, and cardiovascular health. Emotional health variables were also important factors in the alteration of cognition with increasing age; symptoms of depression and anxiety were consistently associated with lower cognitive functioning, whereas self-efficacy was strongly predictive of better cognitive functioning.

Interventions to Enhance Successful Aging

Memory Training Trials With Normal Older Adults

In recent years, evidence has been growing that training or practice can reverse some aspects of age-related cognitive decline or improve performance in persons who have been relatively stable but are disadvantaged relative to younger peers. 6,22,32 Of particular relevance to normal older adults are training programs for age-associated changes in memory.

Memory loss is widely considered the hallmark of age-related decline in our culture and is one of the most common complaints of older persons. Controlled intervention studies generally include instruction in one or more mnemonic techniques to improve memory performance. Most mnemonic techniques involve using mental imagery to create a visual memory cue; for example, in the "method of loci" approach, subjects are asked to imagine a room in their home and to mentally place items from a grocery list at sites around the room. The grocery list items are thus paired with the familiar objects in the room, and this visual paired association enhances list recall. Many memory training programs also include a "pretraining" component, such as relaxation training or teaching semantic elaboration skills to help subjects form associations between a name and a prominent physical characteristic. Pretraining precedes actual mnemonic instruction and is intended to increase participants' treatment gains by providing them with basic skills needed to perform the mnemonic techniques successfully.

A number of studies have shown that memory training can improve memory performance in older persons. Verhaeghen and co-workers reviewed 31 studies in which 1,539 healthy older adults (mean age 60+ years) were taught mnemonic techniques to improve memory performance.³³ A meta-analysis of treatment gains found that treatment gains were larger in mnemonic training groups than in either control or placebo group comparisons. Change scores were also greater when training was conducted in a group (versus individual) format. when pretraining or additional memory-related interventions (such as education on using external memory aids or motivation enhancement) were provided, when subjects were younger, and when sessions were relatively short. Improvement was also greater when the posttreatment outcome was measured with tasks that matched the training condition (for example, a nameface recall task following training in mnemonics for associating names and faces). There were no significant differences in treatment gains with the type or number of mnemonic techniques taught, type of pretraining, number of training sessions, or the presence of an actual trainer (as opposed to getting information from a manual or tape). These findings indicate that older adults can improve their episodic memory, which has implications for some areas of memory function that are important to successful aging, such as remembering important dates, appointments, and phone numbers or recalling names of family and friends.

Stigsdotter and colleagues have examined the longterm maintenance and generalizability of memory training effects.³⁴⁻³⁷ The delayed effects of training were assessed in several studies that observed a total of 42 older adults. In the first, 18 subjects were randomly assigned to one of three conditions: a multifactorial memory training program (that included training in visual imagery, relaxation, and divided-attention tasks), a cognitive activation program (with problem-solving and visual-spatial skills training), or a control group.³⁴ After testing and at six-months assessment, only the subjects in the multifactorial memory training program had substantially improved over baseline on a selective test of reminding word-list recall. In the second study, 24 subjects were assigned to either a multifactorial training program, a unifactorial training group (mnemonic imagery training but no attention or relaxation training), or a control condition.³⁵ Subjects in both the multifactorial and unifactorial groups scored better after testing and at six months than did subjects from the control group, suggesting that the mnemonic training component, not attention or relaxation training, is the active memory-enhancement ingredient.

When subjects from both studies were subsequently retested 3 1/2 years later, all groups scored at the same level as they had at the assessment six months after treatment, indicating the prolonged effect of training.³⁶ Mean scores for the active treatment groups (the multifactorial and unifactorial memory training groups) were significantly higher at the 3 1/2-year follow-up than they had been at pretraining baseline. No improvements were found for subjects in either control group. The combined results from these three studies suggest that memory training can produce long-term effects for older adults, at least for memory tasks that are congruent with the training activity. In a subsequent study with 46 older subjects, the same authors repeated their findings by showing significantly improved and sustained treatment effects for participants in a multifactorial training group compared with controls.³⁷ Improvements were found only for the recall of nouns and concrete objects, however; memory tasks unrelated to the mnemonic (visual imagery) training, such as remembering abstract words or personal activities, were not improved with training. In fact, the authors speculated that training may actually have interfered with subjects' recall on unrelated tasks.

In sum, these studies suggest that older adults can improve their memory performance with training, although the apparent benefit declines with advancing age. Training is most effective for episodic memory tasks that match the training condition. Because there is little evidence that training gains transfer readily to other, untrained memory activities, many of the most important memory tasks of older persons (such as prospective memory for future appointments) may not be affected by traditional memory training approaches. The literature has also provided evidence for the value of memory pretraining and memory-related interventions. The value of these may lie in their effect on older

adults' beliefs about the modifiability of late-life memory skills^{38,39} and on the enhanced sense of control and competence that arises from learning mnemonic skills or effectively using external memory aids.^{40,41}

Lifestyle Changes to Improve Cognition in Normal Older Adults

Based on the review presented earlier, it appears that education, self-efficacy, and physical and psychological health may facilitate or maintain higher cognitive functioning. Conversely, higher cognitive function may facilitate better physical and psychological health. In an early review of normal and successful aging, it was speculated that many of the cognitive losses associated with aging are caused by extrinsic factors (nutrition or personal habits) and are therefore preventable. 42 Consequently, treatments designed to improve self-efficacy, lessen depression and anxiety, and facilitate lifelong learning may well have a beneficial effect on cognitive health.

An area of lifestyle change that deserves particular mention is the current interest in the effects of estrogen levels on cognition in older women and whether estrogen replacement therapy may slow or reverse normal age-related decline. Recent reviews of estrogen supplementation and cognition have found evidence for a positive relationship between estrogen use and verbal memory, concept formation, and reasoning. 43,44 Although these findings have therapeutic implications for successful aging, the demonstrated treatment effects of estrogen on cognition have been modest, raising questions about the relative clinical benefits versus possible medical risks. Only a few studies have looked at the possible long-term effects of estrogen on cognitive function; a greater number have examined the possible secondary influence of estrogen on cognition through its moodenhancing effects, but study findings have frequently been equivocal and contradictory. 43,44 In sum, although estrogen therapy appears to have some promising benefits for maintaining cognitive ability, the literature at present remains investigational, and it would be premature to conclude that estrogen supplements should be routinely prescribed to normal older women for its cognitive-enhancing effects.

Risk Factors for Cognitive Impairment

At the opposite end of the spectrum from successful cognitive aging is the cognitive decline associated with dementing illnesses. The hallmark of dementia is progressive memory loss. Memory loss alone is not sufficient to warrant a diagnosis of dementia, however. Rather, it must be accompanied by other changes in cognition severe enough to interfere substantially with daily functioning, including impairments in judgment, language, motor dexterity, or disturbances of higher executive function such as planning or abstract reasoning.

It is estimated that almost 2 million older adults in this country have severe dementia, and another 1 to 5 million have mild to moderate dementia.⁴⁵ The most common types of progressive late-life dementia are Alzheimer's disease and vascular dementia, which account for more than 75% of the cases of dementia diagnosed in the United States.^{46,47} Other common types include subcortical dementias such as Parkinson's disease or Lewy body diseases, frontal lobe dementia, and dementia resulting from prolonged alcohol abuse.

Just as there are numerous medical causes for the common forms of dementia, so, too, are there various risk factors for their development. For example, the risk factors for vascular dementias are the same as those for vascular disease and stroke, such as hypertension, obesity, diabetes mellitus, hypercholesterolemia, smoking, and lack of exercise. Alzheimer's disease, although less well understood etiologically, is strongly associated with increased age, and there is growing evidence for both genetic and environmental contributing factors. Characterized as an irreversible, degenerative disease with insidious onset and gradually progressive course, Alzheimer's disease affects about 5% of adults older than 65 and between 20% and 50% of persons older than 80.45 Age, however, is neither necessary nor sufficient for the development of Alzheimer's disease. A number of cases of the disease have been reported with onset in young or middle adulthood, and many persons age well into their 80s and 90s without having any signs of dementia.

What then, may differentiate older adults at risk for dementia from those not at risk? Besides age, family history is probably the clearest risk factor for Alzheimer's disease. Genetic studies have led to the identification of gene mutations on chromosomes 1, 14, 19, and 21 that are strongly implicated in familial forms of Alzheimer's disease, ^{48,49} including β -amyloid precursor protein, presenilin-1, presenilin-2, and the ε -4 allele of apolipoprotein E (*APOE-E4*). In fact, recent studies have suggested that increased risk is dose dependent and that the *APOE E4/4* genotype may be associated with an increased risk for accelerated cognitive decline. ⁵⁰

In addition, Alzheimer's disease does not necessarily occur alone. Several recent studies have linked the risk factors for Alzheimer's disease to other diseases. For example, *APOE E4*, the genetic marker discussed earlier, has also been implicated in coronary artery disease. Vascular disease and Alzheimer's disease can coexist: subjects with documented lacunar infarcts (strokes) are at an increased risk for Alzheimer's disease. In addition, diabetes mellitus has been found to increase the risk of dementia threefold.⁵¹

Environmental risk factors for dementia have also been identified, although not as consistently as the genetic markers. Two of these, antioxidants and estrogen, have received particular attention because of their apparent protective effects for Alzheimer's disease. Vitamin E, an antioxidant, has been implicated in a variety of chronic diseases associated with cognitive decline, such as ischemic heart disease, atherosclerosis, diabetes mellitus, and peripheral neuropathies. Although the role of vitamin E in the development of Alzheimer's

disease is still unclear, a recent controlled clinical trial has shown that the use of vitamin E alone (and in conjunction with selegiline hydrochloride [Eldepryl]) can slow the progression of Alzheimer's disease. 52,53 Estrogen is thought to have several mechanisms of action in the brain, including facilitating anticholinergic activity and the growth of cholinergic neurons, enhancing glucose use by brain cells, and maintaining brain cell. Estrogen has also been linked to emotional state, which in turn affects cognitive function. 43 Thus, the role of estrogen in cognitive aging is still unsettled, but it is likely to be multifactorial and important.

Treatments

By far the most successful treatment of dementia occurs when it is determined that cognitive decline is caused by an underlying reversible disorder that can be treated. Hypothyroidism and vitamin B₁₂ deficiency are two of the most common reversible causes found in older adults.⁴⁷ Unfortunately, the most common dementias in elderly persons are the "irreversible" types, dementias with no known cause, such as Alzheimer's disease, or those with causes of limited treatment potential, such as vascular disease.

Because no clear "cause" for Alzheimer's disease has yet been identified, treatment has focused on ameliorating the symptoms, both cognitive and otherwise. Thus far, two "cognitive enhancers" have been approved by the Food and Drug Administration for the treatment of Alzheimer's disease and are currently available: tacrine hydrochloride (Cognex, Parke-Davis) and donepezil (Aricept, Pfizer). Both drugs block the breakdown of acetylcholine, the neurochemical consistently deficient with neurodegenerative cell loss. As noted earlier, selegiline and vitamin E have also been investigated in the treatment of Alzheimer's disease and found to slow the progression of the disease over the course of two years.⁵³ It is also worthwhile to note that a growing body of literature has suggested that both pharmacologic and nonpharmacologic approaches can be effective in reducing the neuropsychiatric and behavioral sequelae of Alzheimer's disease, 54,55 and this may also have implications for improved cognitive function in some affected persons.

Summary and Conclusion

Successful cognitive aging is essential to successful aging as a whole. Numerous definitions have been proposed to describe adequately this important phenomenon. We have followed those that take into account the interactive and multidimensional nature of cognition. Successful cognitive aging is defined as the extent to which a person is able to interact effectively with the environment (both interpersonal and physical) and adapt to age-related changes. Successful older adults, therefore, are the ones who have a minimal interruption of their usual level of function.

Considerable research has been done on the changes in cognition that are associated with aging. Cognition is not unidimensional. Rather, it includes a wide array of verbal and nonverbal skills, including general intellectual ability, memory, language, visual-spatial skills, perception, and complex problem solving. Both crosssectional and longitudinal studies have supported the relative stability of verbal abilities with advancing age and the decline in nonverbal tasks, particularly those involving speed of response. Within this generalization, however, and given the great variation of skills encompassed in the term "cognition," it is not surprising that sizable intraindividual and interindividual differences occur across the age span. Few persons show global decline. Selective maintenance of abilities seems to be the rule rather than the exception.

Several large multivariate epidemiologic studies have consistently implicated the following variables as mitigating factors in the change of cognitive skills with advancing age:

- · Educational level;
- Physical health status, including comorbid medical disease and physical activity; and
- Emotional health status, including depression, anxiety, and perceived self-efficacy.

Randomized controlled clinical trials to enhance successful cognitive aging have focused on age-associated changes in memory. Interventions generally include instruction in one or more mnemonic techniques, and such instruction has been effective in producing targeted, short-term gains. Observed benefits tend to decline with advancing age, however, and whether such gains have functional generalizability remains unknown.

When substantial decline in cognitive abilities occurs, as in the case of the dementing disorders, the causes of such decline are largely unknown. Age is the single strongest predictor of dementia, although age alone is insufficient to predict cognitive decline. A genetic predisposition to decline is the second strongest predictor. Environmental risk factors are also currently being investigated, with particular attention to dietary and hormonal supplements.

We clearly know more now about successful and unsuccessful cognitive aging than we did a scant five years ago, but we have a long way to go. Unanswered questions remain. The best help to our patients is to provide them with our knowledge: some will age successfully, and some will not. For the former, mnemonic training programs offer some hope; for the latter, medications such as tacrine and donepezil and behavioral programs offer respite. In the long run, however, more research is needed to understand how best to predict and enhance successful cognitive aging.

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